

LISTING OF THE CLAIMS

Claim 1 (**currently amended**) A method for the production of a single heavy chain antibody in a non-human mammal comprising the step of expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the VHH heavy chain locus comprises:

(a) ~~at least one VHH region each comprising one~~ VHH exon, at least one ~~D region each comprising one~~ D exon and at least one ~~J region each comprising one~~ J exon, wherein the VHH exonregion, the D exonregion and the J exonregion are capable of recombining to form VDJ coding sequence,

(b) a constant heavy chain region comprising at least one C $\mu$  constant heavy chain gene and at least one of C $\gamma$ , C $\alpha$ , C $\epsilon$ , or C $\delta$  constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

~~which locus when expressed leads to the formation of a single heavy chain antibody~~  
said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claim 2 (**canceled**)

Claim 3 (**currently amended**) A method for the production of a single heavy chain antibody in a non-human mammal comprising the step of expressing a camelised VH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the

camelised VH heavy chain locus comprises:

(a) ~~at least one VH region each comprising one~~ VH exon which is mutated such that, when expressed, the resulting single heavy chain antibody is stabilised, at least one ~~D region each comprising one~~ D exon and at least one ~~J region comprising one~~ J exon, wherein the VH exonregion, the D exonregion and the J exonregion are capable of recombining to form VDJ coding sequence, and

(b) a constant heavy chain region comprising at least one C $\mu$  constant heavy chain gene and at least one of C $\gamma$ , C $\alpha$ , C $\epsilon$ , or C $\delta$  constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

~~which locus when expressed leads to the formation of a single heavy chain antibody~~  
said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen from said mammal.

Claims 4 – 6 (canceled)

Claim 7 (currently amended) A method according to claim 1 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exonregion of human origin and at least one J exonregion of human origin and a constant region of human origin.

Claim 8 (currently amended) A method according to claim 3 wherein the camelised VH heavy chain locus comprises at least one D exonregion of human origin and at least one J exonregion of human origin and a constant region of human origin.

Claim 9 (**canceled**)

Claim 10 (**currently amended**) A method according to claim 1 or [[2]] 3 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 (**original**) A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 (**canceled**)

Claims 17 -32 (**canceled**)

Claim 33 (**previously presented**) The method of claim 1 wherein the entire VHH single heavy chain locus is of camelid origin

Claim 34 (**previously presented**) The method of claim 3 wherein the camelised VH single heavy chain locus is of human origin.

Claim 35 (**previously presented**) The method of claim 3 wherein the camelised VH single heavy chain locus is of non-human origin.

Claim 36 (**previously presented**) The method of claim 3 wherein the camelised VH single heavy chain locus is of camelid origin.

Claims 37 -38 (**canceled**)

Claim 39 (**new**) The method according to claim 1 or 3 wherein the non-human mammal is a rodent.

Claim 40 (**new**) The method according to claim 1 or 3 wherein the regulatory sequence is a locus control region.